Program Announcements (PA'S)

TYPE II OSTEOPOROSIS

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National Institute on Aging
National Institute of Arthritis and Musculoskeletal and Skin Diseases

BACKGROUND

Osteoporosis and associated fractures constitute a major public health problem affecting more than 20 million Americans. Osteoporosis can be defined as an absolute decrease in the amount of bone, leading to fractures after minimal trauma. While women are disproportionately vulnerable to this debilitating disease, both men and women lose bone mineral with age and are at increasing risk for fracture as they grow older. One third of women over 65 years of age will suffer vertebral fractures. By age ninety, one third of the women and approximately 17 percent of the men will have experienced a hip fracture.

Although the fundamental pathogenesis of osteoporosis remains unclear, clinical evidence suggests that there are two types of the syndrome. Type I, which occurs mainly in women within 15 to 20 years after menopause, is manifested by vertebral crush fracture and Colles' fracture of the distal forearm. Type II osteoporosis occurs in both men and women over the age of 70 and is associated mainly with hip, pelvic, proximal femur, and wedge type vertebral fractures.

Clinically, type I and II are not readily distinguishable and both often occur in the same patient. However, there are a number of characteristics which help to distinguish them. Type I osteoporosis is associated with excessive and disproportionate loss of trabecular bone, but the rate of cortical-bone loss is only slightly above usual age-related rates. It is also closely related to factors associated with menopause, and the most effective method to date of reducing postmenopausal bone loss is estrogen therapy.

In the type II form of osteoporosis, bone loss is proportionate for both cortical and trabecular bone and is only slightly greater for patients with fracture than for the remainder of the aging population. As bone is lost, increasing numbers of older people have bone densities that fall below the fracture threshold. Age-related risk factors include decreased osteoblast function and impaired 1,25(OH)2D, leading to decreased calcium absorption and secondary hyperparathyroidism. At

present, there is no established universally effective therapy for type II osteoporosis.

GOALS AND SCOPE

Much recent osteoporosis research has been directed toward the postmenopausal, type I form. Both epidemiologic and clinical findings suggest that type II and type I osteoporosis may be related but they are not identical. The goal of this announcement is to encourage research to determine whether these two syndromes of osteoporosis have different etiologic mechanisms and to develop theories of pathogenesis which can lead to the prediction, prevention, and treatment of type II osteoporosis. This research lends itself to interdisciplinary collaboration in the areas of cell biology, biochemistry, endocrinology, physiology, biophysics, epidemiology, and aging. The NIA/NIAMS encourages collaborative proposals from experimental gerontologists, geriatricians, bone endocrinologists and related biomedical researchers.

The NIH urges applicants for grants to give added attention (where feasible and appropriate) to the inclusion of minority groups and/or women in the study populations for research.

SPECIFIC OBJECTIVES

The NIA/NIAMS invite grant applications to test hypotheses and elucidate mechanisms including, but not limited to, the following general areas:

Etiologic mechanisms underlying type II osteoporosis in men and women. Suspected factors include parathyroid function, calcium absorption, vitamin D metabolism, bone remodeling, prostaglandin and growth factor activity, and osteoblast function.

The role of age-related changes in bone biochemistry, bone turnover, bone cells, endocrine function, mineral absorption, and other aging changes in contributing to age-related bone loss in men and women.

Improved techniques for measuring bone density and bone strength, and their validation in old and very old persons.

Epidemiologic studies designed to determine risk factors for type II osteoporosis in men and women. Longitudinal studies are particularly encouraged. Incidence and prevalence studies among races and ethnic groups which may offer mechanistic explanations of type II osteoporosis are also encouraged.

Interventions that may prevent or retard age-related osteoporosis in men and women including exercise, diet, drug and/or hormonal therapy as well as other factors that are linked to type II disease.

MECHANISMS OF RESEARCH SUPPORT

The primary mechanisms for support of this program are:

Research Project Grant (RO1)

FIRST Award (R29)

Career grants, which include: Special Emphasis Research Career Award (K01) in Nutritional and Metabolic Factors in Aging Research Career Development Award (K04) Clinical Investigator Award (KO8) Academic Award (K08)

REVIEW PROCEDURES

Applications will be evaluated in accordance with the usual NIH peer review procedures, based on scientific merit. Following study section review, the applications will be evaluated by the National Advisory Council on Aging and the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council. Awards will be based on available funds.

METHOD OF APPLYING

Applications should be submitted on the PHS 398 (Revised 9/86) application form. Application deadlines are February 1, June 1, or October 1. Under item 2, on the face page of the application, Response To Specific Program Announcement, type NIA/NIAMS, TYPE II (AGE-RELATED) OSTEOPOROSIS. If your institution does not have NIH research grant application kits, copies may be obtained by writing:

Office of Grant Inquiries Division of Research Grants National Institutes of Health Westwood Building, Room 449 Bethesda, Maryland 20892 Telephone: (301) 496-7441

Forward the original + 6 copies of the completed application to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20892**

INQUIRIES AND CORRESPONDENCE

Potential applicants interested in obtaining further information may call:

Ann W. Sorenson, Ph.D.
Osteoporosis and Rheumatology Program Director
National Institute on Aging
Bethesda, Maryland 20892
Telephone: (301) 496-1033

Stephen L. Gordon, Ph.D.
Musculoskeletal Diseases Program Director
National Institute of Arthritis and
Musculoskeletal and Skin Diseases
Westwood Building, Room 405
Bethesda, Maryland 20892
Telephone: (30l) 496-7326